IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of: Robert C. GETTS et al.	:	
Application No.: 09/908,950	:	Group Art Unit: 1637
Filed: July 19, 2001	:	Examiner: Chunduru, Suryaprabha
For: METHODS FOR DETECTING AND ASSAYING NUCLEIC ACID SEQUENCES	:	Confirmation No.: 1927
	:	X

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

Sir:

Further to the Notice of Appeal filed on January 20, 2010, for the subject application, a brief in support of the appeal is now submitted. Submission of a brief in support of the appeal in this case was due by March 20, 2010. Accordingly, a petition to extend the period for an additional one (1) month is also being submitted herewith.

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REAL PARTY IN INTEREST

The real party in interest is Genisphere, LLC, the assignee of record.

RELATED APPEALS AND INTERFERENCES

The undersigned is not aware of any appeals or interferences that are related to this appeal, or which will affect or have a bearing on this appeal.

STATUS OF CLAIMS

Claims 1-58 were finally rejected in the Office Action mailed on September 11, 2009, and are the subject of this appeal.

STATUS OF AMENDMENTS

No claims have been amended, added or cancelled subsequent to the Final Office Action.

SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter encompasses devices for use in assays. Independent claim 1 is directed to a method for determining the presence of a specific nucleotide sequence in RNA of a target sample, comprising the steps of:

a) incubating a mixture comprising: (*page 7, line7*)

(i) a first component including RNA extracted from a target sample, said RNA having a target nucleotide sequence and a capture sequence, (*page 7, line 8-10*) and

(ii) a second component comprising a capture reagent, said capture reagent comprising multiple first arms and multiple second arms, said first arms being arms comprising a label capable of emitting a detectable signal, said second arms being arms comprising a nucleotide sequence complementary to the capture sequence of said RNA of the first component, (*page 7, lines 11-14*)

at a first temperature to induce the capture sequence of said RNA of the first component to bind to the complementary nucleotide sequence of the capture reagent of the second component, and thereby forming a pre-hybridized RNA-capture reagent complex comprising the target nucleotide sequence; (*page 7, lines15-19*)

b) contacting the pre-hybridized RNA-capture reagent complex with a microarray having thereon a plurality of

features each comprising a particular probe nucleotide sequence; (*page 7, lines 20-22*) and

c) incubating the pre-hybridized RNA-capture reagent complex on the microarray at a second temperature to hybridize the target nucleotide sequence of the pre-hybridized RNA capture reagent complex to the complementary probe nucleotide sequence contained within the feature, wherein the presence of such hybridization results in a detectable hybridization pattern for subsequent analysis. (*page 7, line 23 to page 8, line 6*)

Independent claim 19 is directed to a method for determining the presence of a specific nucleotide sequence in RNA of a target sample, said method comprising the steps of:

a) contacting a first component with a microarray having thereon a plurality of features each comprising a particular probe nucleotide sequence, said first component including RNA extracted from a target sample, said RNA having a target nucleotide sequence and a capture sequence; (*page 8, lines 11-14*)

b) incubating said RNA and the complementary probe nucleotide sequences on the microarray at a first temperature to hybridize the target nucleotide sequence of

said RNA to the complementary probe nucleotide sequence contained within the feature; (*page 8, lines 15-18*)

c) taking a second component comprising a capture reagent, said capture reagent comprising multiple first arms and multiple second arms, said first arms being arms comprising a label capable of emitting a detectable signal, said second arms being arms comprising a nucleotide sequence complementary to the capture sequence of said RNA of the first component; (*page 8, lines 19-22*) and

d) incubating the capture reagent and the capture sequence of said RNA at a second temperature to induce the capture sequence of said RNA of the first component to hybridize to the complementary nucleotide sequence of the capture reagent of the second component, wherein the presence of the hybridization results in a detectable hybridization pattern for subsequent analysis. (*page 8, line 22 to page 9, line 6*)

Independent claim 47 is directed to a method comprising the steps of:

(a) taking an array of probe nucleotide sequences; (*Fig. 2, "icroarray"*

(b) taking a first component comprising RNA, said RNA having a target nucleotide sequence and a capture sequence; (*Fig. 2, "RNA"*

(c) taking a second component comprising multiple arms, said arms each comprising a complement, said complement being a complementary nucleotide sequence to said capture sequence of said RNA; (*Fig. 2, "dendrimer"*)

(d) contacting said RNA with both said array and said second component in any order; (Fig. 2, *"mRNA/dendrimer hybridization"*)

(e) wherein said RNA is contacted with said array to allow said target nucleotide sequence of said RNA to bind to any of said probe nucleotide sequences on said array that comprise DNA or RNA complementary to said target nucleotide sequence; (Fig. 2, *"mRNA/dendrimer hybridization"*)

(f) wherein said RNA is contacted with said second component to allow said complement to bind to said capture sequence of said RNA; (Fig. 2, *"mRNA/dendrimer hybridization"*)

(g) and wherein said second component produces a detectable hybridization pattern on said array. (Fig. 2, *"scan microarray"*)

Independent claim 52 is directed to a composition comprising:

(a) an array of probe nucleotide sequences; (*Fig. 2, microarray*)

(b) said array further comprising a first component comprising RNA, said RNA having a target nucleotide sequence and a capture sequence, said target nucleotide sequence of said RNA being bound to one of said probe nucleotide sequences on said array, wherein said target sequence of said RNA is bound to a probe nucleotide sequence of DNA or RNA; (*Fig. 2, mRNA*)

(c) said composition further comprising a second component, said second component comprising multiple arms, said arms each comprising a complementary nucleotide sequence to said capture sequence of said RNA, said complementary nucleotide sequence being bound to said capture sequence; (*Fig. 2, dendrimer*)

(d) and wherein said second component further comprises a label. (*Fig. 2, fluorescent probe*)

The dependent claims are directed to various embodiments of the disclosed methods and compositions.

A copy of the appealed claims is appended hereto, beginning at page 22.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL[1]

I. Whether claims 1-3, 7, 8, 17, 18-22 25, 26 and 35-58 are unpatentable under 35 U.S.C. § 103(a) over Skouv, US 6,303,315 ("Skouv") in view of Gerhart et al., J. Cell Biol. 149, 2000, 825-833 ("Gerhart").

II. Whether claims 4-6, 9-16, 23, 24 and 27-34 are unpatentable under 35 U.S.C. § 103(a) over Skouv in view of Gerhart, and further in view of Van Ness et al., US 6,361,940 ("Van Ness").

[1] Claims 1-5, 9-17, 19-23, 27-36, 43 and 49 were also provisionally rejected for obviousness-type double patenting over the claims of co-pending U.S. Patent Application No. 09/802,162. This rejection is not appealed, and upon indication of one or more allowable claims following conclusion of this appeal, Appellants will address the rejection as appropriate.

ARGUMENT

I. Skouv in view of Gerhart

Claims 1-3, 7, 8, 17-22 25, 26 and 35-58 stand finally rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Skouv in view of Gerhart. According to the Examiner in the Office Action mailed on October 16, 2008:

> Skouv teaches a method and composition of claims 1, 19, 47, 50 comprising incubating a first component comprising RNA extracted from a sample said RNA comprising a capture sequence and a target specific sequence (see col. 10, line 37-41, col. 7, line 44-56, col. 3, line 32-61); and hybridizing said first component with a microarray comprising plurality of probes (see col. 5, line 27-46) and incubation at a temperature that facilitates hybridization and detecting the hybridization pattern (see col. 9, line 14-50).
> …
>
> However Skouv did not specifically teach dendrimers having multiple arms.
>
> Gerhart et al. teach a nucleic acid detection method comprising the use of dendrimers having multiple single-stranded arms (see page 825, col. 2, paragraph 1, page 826, Fig. 1, col. 1, line 1-13). Gerhart et al. also teach that the dendimer comprises multiple first arms comprising a label and second arms comprising target specific sequences complementary to capture RNA (see page 826, col. 1, paragraph 2 under materials and methods).
>
> Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method for detecting a nucleic acid as taught by Skouv with a dendrimer having multiple arms as taught by Gerhart et al. to achieve expected advantage of developing an enhanced sensitivity of detecting a target nucleic acid.

Appellants maintain that the combination of Skouv in view of Gerhart would not have suggested the subject matter of claims 1-3, 7, 8, 17-22 25, 26 and 35-58. In

rejecting claims under 35 U.S.C. § 103, it is incumbent upon the Examiner to establish a factual basis to support the legal conclusion of obviousness. *See In re Fine*, 837 F.2d 1071, 1073 (Fed. Cir. 1988). In so doing, the Examiner must make the factual determinations set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966), *viz.*, (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; and (3) the level of ordinary skill in the art. "[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). To establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 985 (CCPA 1974). Furthermore, although the analysis need not identify explicit teachings directed to the claimed subject matter, "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). As such, "'there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *Id.* (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

Claims 1-3, 7, 8, 17, 18-22 25, 26 and 35-58 in General

Each of claims 1, 19, 47 and 52 (the only independent claims on appeal) requires, *inter alia*, a RNA having a target nucleotide sequence and a capture sequence, a second component comprising a labeled capture reagent complementary to the capture sequence, and a microarray containing a plurality of probes complementary to the target nucleotide sequence. As explained in the subject application, the ability to directly detect RNA on a

microarray avoids the time- and labor-consuming enzymatic conversion of RNA into cDNA. *See* page 10, lines 3-14.

Skouv does not teach or suggest such a RNA/capture reagent/microarray system. Skouv is directed to a method for simultaneous release and detection of nucleic acids from a biological sample through the combined use of strong chaotropic agents and locked nucleic acids (LNAs). *See* Abstract. The method includes lysing the cells in a hybridization medium comprising a strong chaotropic agent, contacting the lysate under hybridization conditions with a LNA having a nucleotide sequence substantially complementary to a nucleotide sequence suspected to be present in the cells, and determining the extent of hybridization. *See* col. 3, lines 24-31. According to Skouv, solutions containing high concentrations of guanidine, guanine thiocyanate or certain other chaotropic agents and detergents are capable of effectively lysing prokaryotic and eukaryotic cells while simultaneously allowing specific hybridization of LNA probes to the released endogenous nucleic acid. The solutions need not contain any other component other than common buffers and detergents to promote lysis and solubilization of cells and nucleic acid hybridization. *See* col. 4, lines 19-27.

At col. 5, lines 27-39, Skouv discusses the following possibility:

> An attractive possibility of the invention is the use of different LNA-oligomers directed against different sequences in the genome which are spotted in an array format and permanently affixed to the surface (Nature Genetics, suppl. vol. 21, January 1999, 1-60 and WO 96/31557). Such an array can subsequently be incubated with the mixture of the lysis buffer/hybridisation medium containing dissolved cells and a number of suitable detection LNA-probes. The lysis and hybridisation would then be allowed to occur, and finally the array would be washed and appropriately developed. The result of such a

procedure would be a semi-quantitative assessment of a large number of different target nucleic acids.

Thus, Appellants acknowledge that Skouv arguably discloses a microarray-based method of identifying a nucleotide sequence in a target biological sample. However, the method disclosed in Skouv is fundamentally different from the method recited in the instant claims. Figure 2 of the subject application, reproduced below, illustrates the basic claimed method.

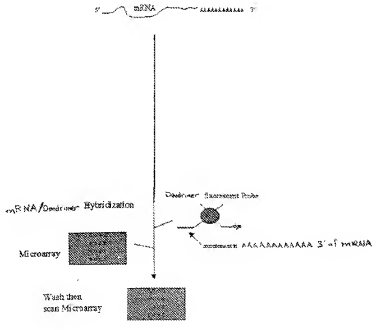

FIGURE 2

As shown, a first component comprising RNA (in this case, mRNA) having a target nucleotide sequence and a capture sequence (in this case, a poly(A) sequence) is hybridized to a second component (in this case, a dendrimer) comprising a labeled capture reagent comprising a nucleotide sequence complementary to the capture sequence (in this case, a poly(T) sequence). The RNA/capture reagent complex is then hybridized

to a microarray containing a plurality of probes, resulting in a detectable hybridization pattern for subsequent analysis.

Thus, the claimed invention requires at least a capture sequence on an RNA, a labeled capture reagent and a plurality of microarray probes. Although Skouv uses the term "capturing" nucleic acid, this is in reference to the LNA probes which may be covalently attached to a solid support. *See* col. 6, line 66 to col. 7, line 3. Since this can be considered analogous to the microarray probes recited in the instant claims, there is no description in Skouv of a labeled capture reagent capable of hybridizing to a capture sequence on an RNA.

Furthermore, each of the instant requires a specific type of capture reagent, namely a capture reagent comprising multiple first arms and multiple second arms, the first arms comprising a label capable of emitting a detectable signal, and the second arms comprising a nucleotide sequence complementary to the capture sequence on the RNA. According to the Examiner, one of skill in the art would have been motivated to modify the method of Skouv with a dendrimer having multiple arms as taught by Gerhart to achieve expected advantage of developing an enhanced sensitivity of detecting a target nucleic acid. However, this conclusion ignores the fact that the dendrimer in Gerhart had a second arm comprising a nucleotide sequence complementary to a specific *target* sequence in RNA (MyoD, myosin, G3PDH), rather than a common capture sequence. *See* page 826, second column. The great benefit of Appellants' method is that a single capture sequence can be used for labeling of all RNA/microarray hybridization events. This is not suggested by Gerhart. Thus, one of skill in the art would not have been motivated to replace the "signal" nucleic acids in Skouv with the dendrimer in Gerhart, as

suggested by the Examiner, for if such a replacement were attempted, it would result in an inoperable assay.

Accordingly, Appellants maintain that claims 1-3, 7, 8, 17, 18-22 25, 26 and 35-58 are not unpatentable over Skouv in view of Gerhart, and reversal of the rejection is respectfully requested.

Claim 7, 8, 25, 26, 51 and 56

Claims 7, 8, 25, 26, 51 and 56 depend from claims 1, 19, 47 or 52 and further require that the capture sequence on the RNA comprise or consist of a polyA sequence. According to the Examiner, Skouv teaches that the capture sequence of said RNA is single stranded oligonucleotide consisting of polyA sequence and a sequence that is complementary to the capture sequence comprises at least one thymine base (see col. 10, line 37-41, col. 7, line 44-56, col. 3, line 32-61, col. 17, line 15-23). However, none of these passages specifically teach that the capture sequence of an RNA, to which the capture reagent must hybridize comprises or consists of a polyA sequence. Although mRNA may inherently contain a polyA tail, nothing in Skouv suggests that the "signal" nucleic acid is directed to this portion of the RNA. Furthermore, as discussed above, the dendrimer in Gerhart had a second arm comprising a nucleotide sequence complementary to a specific *target* sequence in RNA (MyoD, myosin, G3PDH), rather than a common polyA capture sequence. Also, nothing in Skouv teaches or suggests that the sequence complementary to the capture sequence comprises at least one thymine base. The portion of Skouv relied upon by the Examiner (col. 17, lines 15-23) actually states that the LNA probe (analogous to the microarray probes recited in the instant claims) preferably

contains a thymine. No mention is made in Skouv whether such a preference exists for the "signal" nucleic acid.

Accordingly, Appellants maintain that claims 7, 8, 25, 26, 51 and 56 are not unpatentable over Skouv in view of Gerhart independent of the reasons given above regarding claims 1-3, 7, 8, 17-22 25, 26 and 35-58 in general, and reversal of the rejection is respectfully requested.

II. Skouv in view of Gerhart, further in view of Van Ness

Claims 4-6, 9-16, 23, 24 and 27-34 stand finally rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Skouv in view of Gerhart as applied to claims 1-3, 7, 8, 17-22, 25, 26 and 35-58 above, further in view of Van Ness. The Examiner acknowledges in the Office Action mailed on October 16, 2008, that neither Skouv nor Gerhart teach hybridization temperatures ranging from 50-60° C, incubation time, and base solution to separate and purge the hybridized RNA reagent, but states that Van Ness teaches a method for enhancing hybridization and probing or priming specificity with the recited parameters.

Claims 4-6, 9-16, 23, 24 and 27-34 depend from claims 1 or 19. As discussed above with respect to these claims, Skouv in view of Gerhart would not have suggested hybridization of multiple armed capture reagent to a capture sequence on RNA for use in detection of probes on a microarray. The Examiner has pointed to nothing in Van Ness that remedies the deficiencies of Skouv and Gerhart in this respect. As such, the combination of Van Ness with Skouv and Gerhart cannot render the claimed invention obvious. *See In re Rijckaert*, 9 F.3d 1531, 1533 (Fed Cir. 1993).

Furthermore, with regard to claims 4-6 and 22-24, wherein a base solution is passed over the microarray to separate and purge the hybridized RNA from the probe nucleotide sequence for enabling reuse of the microarray, the Examiner's citation to column 66, lines 10-14 of Van Ness does not disclose such a step. That portion of Van Ness merely states that the RNA of cDNA/RNA duplex can by hydrolyzed with a base. Such a teaching has no relevance to the hydrolysis of RNA on a microarray, particularly where cDNA synthesis is not performed.

Accordingly, Appellants maintain that claims 4-6, 9-16, 23, 24 and 27-34 are not unpatentable over Skouv in view of Gerhart, further in view of Van Ness, and reversal of the rejection is respectfully requested.

CONCLUSION

For the foregoing reasons, Appellants maintain that claims 1-58 of the instant application meet the requirements for patentability under 35 U.S.C. §§ 101 *et seq.* Accordingly, reversal of the Examiner's rejections is appropriate and is respectfully solicited. Please note new counsel's correspondence address and docket number set forth herein.

Dated: April 20, 2010

Respectfully submitted,

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CLAIMS APPENDIX

1. A method for determining the presence of a specific nucleotide sequence in RNA of a target sample, said method comprising the steps of:

a) incubating a mixture comprising:

(i) a first component including RNA extracted from a target sample, said RNA having a target nucleotide sequence and a capture sequence, and

(ii) a second component comprising a capture reagent, said capture reagent comprising multiple first arms and multiple second arms, said first arms being arms comprising a label capable of emitting a detectable signal, said second arms being arms comprising a nucleotide sequence complementary to the capture sequence of said RNA of the first component,

at a first temperature to induce the capture sequence of said RNA of the first component to bind to the complementary nucleotide sequence of the capture reagent of the second component, and thereby forming a pre-hybridized RNA-capture reagent complex comprising the target nucleotide sequence;

b) contacting the pre-hybridized RNA-capture reagent complex with a microarray having thereon a plurality of features each comprising a particular probe nucleotide sequence; and

c) incubating the pre-hybridized RNA-capture reagent complex on the microarray at a second temperature to hybridize the target nucleotide sequence of the pre-hybridized RNA capture reagent complex to the complementary probe nucleotide sequence contained within the feature, wherein the presence of such hybridization results in a detectable hybridization pattern for subsequent analysis.

2. The method of claim 1 wherein the capture reagent is selected from the group consisting of dendrimers, carbohydrates, proteins, and nucleic acids.

3. The method of claim 2 wherein the capture reagent is a dendrimer.

4. The method of claim 1 further comprising passing a base solution over the microarray to separate and purge the hybridized RNA from the probe nucleotide sequence for enabling reuse of the microarray.

5. The method of claim 4 wherein the base solution is passed over the microarray at a temperature of from about 50º to 60º C.

6. The method of claim 4 wherein the base solution is 0.05 M sodium hydroxide.

7. The method of claim 1 wherein the capture sequence of said RNA is a single-stranded oligonucleotide consisting of a poly dA sequence.

8. The method of claim 7 wherein the nucleotide sequence complementary to the capture sequence is a single-stranded oligonucleotide consisting of at least one thymine base.

9. The method of claim 1 wherein said RNA and the capture reagent are incubated at the first temperature of from about 45° to 60° C.

10. The method of claim 9 wherein said RNA and the capture reagent are incubated for a sufficient time ranging from about 15 minutes to 24 hours.

11. The method of claim 1 wherein the pre-hybridized RNA-capture reagent complex is incubated on the microarray at the second temperature of from about 45° to 65° C.

12. The method of claim 11 wherein the pre-hybridized RNA-capture reagent complex are incubated on the microarray for the sufficient time ranging from about 15 minutes to 24 hours.

13. The method of claim 11 wherein the probe nucleotide sequences of the microarray comprises cDNA.

14. The method of claim 11 wherein the second temperature is from about 60° to 65° C.

15. The method of claim 11 wherein the probe nucleotide sequences of the microarray comprises oligonucleotides.

16. The method of claim 14 wherein the second temperature is from about 45° to 55° C.

17. The method of claim 1, further comprising washing any free unhybridized RNA-capture reagent complex from the microarray after incubating the pre-hybridized RNA-capture reagent complex on the microarray.

18. The method of claim 1, further comprising adding blocking nucleic acids to the mixture of the first and second components after incubation of the first and second components.

19. A method for determining the presence of a specific nucleotide sequence in RNA of a target sample, said method comprising the steps of:

a) contacting a first component with a microarray having thereon a plurality of features each comprising a particular probe nucleotide sequence, said first component including RNA extracted from a target sample, said RNA having a target nucleotide sequence and a capture sequence;

b) incubating said RNA and the complementary probe nucleotide sequences on the microarray at a first temperature to hybridize the target nucleotide sequence of said RNA to the complementary probe nucleotide sequence contained within the feature;

c) taking a second component comprising a capture reagent, said capture reagent comprising multiple first arms and multiple second arms, said first arms being arms comprising a label capable of emitting a detectable signal, said second arms being arms comprising a nucleotide sequence complementary to the capture sequence of said RNA of the first component; and

d) incubating the capture reagent and the capture sequence of said RNA at a second temperature to induce the capture sequence of said RNA of the first component to hybridize to the complementary nucleotide sequence of the capture reagent of the second component, wherein the presence of the hybridization results in a detectable hybridization pattern for subsequent analysis.

20. The method of claim 19 wherein the capture reagent is selected from the group consisting of dendrimers, carbohydrates, proteins, and nucleic acids.

21. The method of claim 20 wherein the capture reagent is a dendrimer.

22. The method of claim 19 further comprising passing a base solution over the microarray to separate and purge the hybridized RNA from the probe nucleotide sequence for enabling reuse of the microarray.

23. The method of claim 22 wherein the base solution is passed over the microarray at a temperature of from about 50° to 60° C.

24. The method of claim 22 wherein the base solution is 0.05 M sodium hydroxide.

25. The method of claim 19 wherein the capture sequence of said RNA is a single-stranded oligonucleotide consisting of a poly dA sequence.

26. The method of claim 25 wherein the nucleotide sequence complementary to the capture sequence is a single-stranded oligonucleotide consisting of at least one thymine base.

27. The method of claim 19 wherein said RNA and the complementary probe nucleotide sequences on the microarray are incubated at the first temperature of from about 45° to 65° C.

28. The method of claim 27 wherein said RNA and the complementary probe nucleotide sequences on the microarray are incubated for a sufficient time ranging from about 15 minutes to 24 hours.

29. The method of claim 27 wherein the probe nucleotide sequences of the microarray comprises cDNA.

30. The method of claim 29 wherein the first temperature is from about 60° to 65° C.

31. The method of claim 27 wherein the probe nucleotide sequences of the microarray comprises oligonucleotides.

32. The method of claim 31 wherein the second temperature is from about 45° to 55° C.

33. The method of claim 19 wherein the capture reagent and the capture sequence of the RNA are incubated at a second temperature ranging from about 45° to 60° C.

34. The method of claim 33 wherein the capture reagent and the capture sequence of the RNA are incubated for the sufficient time ranging from about 15 minutes to 24 hours.

35. The method of claim 19, further comprising adding blocking nucleic acids to the microarray after incubating the capture sequence of the RNA and the capture reagent on the microarray.

36. The method of claim 19, further comprising washing the microarray with a buffer solution to remove excess unhybridized RNA after the incubating said RNA and the complementary nucleotide probes on the microarray step.

37. The method of claim 1 wherein the capture sequence of said RNA comprises at least one locked nucleic acid nucleotide.

38. The method of claim 19 wherein the capture sequence of said RNA comprises at least one locked nucleic acid nucleotide.

39. The method of claim 1, wherein said probe nucleotide sequence is DNA.

40. The method of claim 1, wherein said probe nucleotide sequence is RNA.

41. The method of claim 19, wherein said probe nucleotide sequence is DNA.

42. The method of claim 19, wherein said probe nucleotide sequence is RNA.

43. The method of claim 1, wherein said second component comprises a capture reagent having at least one first arm comprising said label and at least one second arm having comprising said nucleotide sequence complementary to said capture sequence of said RNA.

44. The method of claim 43, wherein said second component is a dendrimer.

45. The method of claim 19, wherein said second component comprises a capture reagent having at least one first arm comprising said label and at least one second arm having comprising said nucleotide sequence complementary to said capture sequence of said RNA.

46. The method of claim 45, wherein said second component is a dendrimer.

47. (Previously Presented) A method comprising the steps of:

(a) taking an array of probe nucleotide sequences;

(b) taking a first component comprising RNA, said RNA having a target nucleotide sequence and a capture sequence;

(c) taking a second component comprising multiple arms, said arms each comprising a complement, said complement being a complementary nucleotide sequence to said capture sequence of said RNA;

(d) contacting said RNA with both said array and said second component in any order;

(e) wherein said RNA is contacted with said array to allow said target nucleotide sequence of said RNA to bind to any of said probe nucleotide sequences on said array that comprise DNA or RNA complementary to said target nucleotide sequence;

(f) wherein said RNA is contacted with said second component to allow said complement to bind to said capture sequence of said RNA;

(g) and wherein said second component produces a detectable hybridization pattern on said array.

48. The method of claim 47, wherein said second component comprises a dendrimer.

49. The method of claim 47, wherein said second component comprises at least one molecule selected from the group consisting of dendrimers, carbohydrates, proteins, and nucleic acids.

50. The method of claim 47, wherein said capture sequence comprises at least one LNA (Locked Nucleic Acid) nucleotide.

51. The method of claim 47, wherein said capture sequence comprises a poly dA sequence.

52. A composition, said composition comprising:

(a) an array of probe nucleotide sequences;

(b) said array further comprising a first component comprising RNA, said RNA having a target nucleotide sequence and a capture sequence, said target nucleotide sequence of said RNA being bound to one of said probe nucleotide sequences on said array, wherein said target sequence of said RNA is bound to a probe nucleotide sequence of DNA or RNA;

(c) said composition further comprising a second component, said second component comprising multiple arms, said arms each comprising a complementary nucleotide sequence to said capture sequence of said RNA, said complementary nucleotide sequence being bound to said capture sequence;

(d) and wherein said second component further comprises a label.

53. The composition of claim 52, wherein said second component comprises a dendrimer.

54. The composition of claim 52, wherein said second component comprises at least one molecule selected from the group consisting of dendrimers, carbohydrates, proteins, and nucleic acids.

55. The composition of claim 52, wherein said capture sequence comprises at least one LNA (Locked Nucleic Acid) nucleotide.

56. The composition of claim 52, wherein said capture sequence comprises a poly dA sequence.

57. A method as claimed in claim 47, further comprising the step of adding a ribonuclease inhibitor to protect said RNA.

58. A method as claimed in claim 47, further comprising the step of conducting dual channel analysis on said array.

EVIDENCE APPENDIX

None.

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RELATED PROCEEDINGS APPENDIX

None.